

Attorney Docket No.: RU-0130  
Inventors: Yurkow and Mermelstein  
Serial No.: 09/913,435  
Filing Date: February 2, 2002  
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#### REMARKS

While the Examiner states claims 1-5 are pending, it is respectfully noted that claims 2-4 were canceled on April 16, 2004 and, in fact, claims 1 and 5 are pending in the instant application. Claims 1 and 5 have been rejected. No new matter has been added by this amendment. Reconsideration is respectfully requested in light of the following remarks.

#### I. Rejection Under 35 U.S.C. 102

Claims 1 and 5 have been rejected under 102(b) as being anticipated by Qui et al. ((1996) *J. Biol. Chem.* 271:31915-31921). It is suggested that Qui et al. teach a method of stabilizing or maintaining the redox state of hypoproliferative human colonic carcinoma cells, cell line HCT116, by contact the cells with chemotherapeutic agents, aziridinybenzoquinones, and a redox clamping agent, N-acetylcysteine. It is suggested that this reference teaches redox cycling in abnormal growth or proliferation and that the effect of N-acetylcysteine on free radical production by the quinines suggests effective transfer of the radical character from an oxygen-centered radical to a less reactive sulfur-center radical (Reaction 2). Applicants respectfully traverse rejection.

Qui et al. disclose the mechanism of action of aziridinybenzoquinones. This reference teaches that the metabolism of aziridinybenzoquinones generates oxygen radicals. In turn, these oxygen radicals induce expression of the cell cycle inhibitor p21 whose overexpression suppresses the growth of tumor cells. See first and third paragraph of the abstract. Qui et al. further teach inhibiting aziridinybenzoquinone-mediated

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induction of p21 using the antioxidant N-acetylcysteine. See page 31917, column 2, 4<sup>th</sup> full paragraph. This inhibition of p21 induction is suggested to result from oxidation of the thiol of N-acetylcysteine by the free radicals formed during the metabolism of the aziridinybenzoquinones. In this regard, Qui et al. fail to teach stabilizing abnormal fluctuations in the redox state associated with abnormal cell growth or proliferation because the abnormal redox state of the cells of Qui et al. was associated with free radicals *formed during the redox transitions of the aziridinybenzoquinones*. Moreover, this reference fails to teach sensitizing non-viral cells to the effects of a chemotherapeutic agent using a redox clamping agent because the antioxidant of Qui et al. blocks the aziridinybenzoquinones-mediated induction of p21. Accordingly, this reference fails to teach each and every element of the instant claims and therefore fails to anticipate the present invention. It is therefore respectfully requested that this rejection be withdrawn.

## **II. Objection to the Title**

The title has been objected to as not being descriptive of the invention. A new title is required that is clearly indicative of the invention which is claimed. Accordingly, Applicants have amended the title of the invention to describe the methods being claimed. Withdrawal of this objection is respectfully requested.

## **III. Conclusion**

The Applicants believe that the foregoing comprises a full and complete response to the Office Action of record.

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Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,



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